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Epidemiologic Patterns of Colorectal Cancer

10

Introduction ■

Magnitude of the Problem ■

In the United States today the incidence and mortality rates for colorectal cancer are second only to those for lung cancer. In 1985 an estimated 138,000 new cases were diagnosed, 70% in the colon and 30% in the rectum, and an estimated 59,900 deaths occurred.[1] Colorectal cancer constitutes about 15% of all newly diagnosed cancers, if nonmelanoma skin cancers and various carcinomas *in situ* are excluded, and 13% of all cancer deaths. At present the probability of a white female developing colorectal cancer during her lifetime is 6.8% and of dying from it, 3.1%. The probability of a white male developing colorectal cancer during his lifetime is 6.3% and of dying from it, 2.9%.[2]

Etiologic Leads ■

Diet appears to contribute to several forms of cancer,[3] with the evidence being especially provocative for colorectal cancer. Two major risk factors for colorectal cancer are thought to be diets low in fiber and high in fat, but the mechanisms appear complex and difficult to unravel. For example, dietary fat increases the secretion of bile acids and neutral steroids, which may promote colon carcinogenesis; it may also alter the bacterial degradation of these acid and neutral steroids so that specific carcinogens are formed.[4,5] High consumption of meat and animal protein may increase risk independent of high fat intake through the formation of carcinogenic amino acid degradation products in the large bowel[5,6] or through carcinogens produced by broiling or frying meat at high temperatures.[7] Mutagenic activity in the feces is more prevalent in populations at high risk of colorectal cancer,[8] and fecal mutagens called fecapentaenes have now been characterized.[9]

Dietary fiber, the portion of ingested carbohydrate that is not digested in the small intestine and enters the large intestine, may provide bulk to dilute the concentration of fecal carcinogens and speed their transit through the bowel.[10] Fiber may also sequester carcinogens in the large bowel and limit their activity[11] or modify the bacterial flora and the degradation products formed.[12] In recent years the chemical composition of the heterogeneous components of dietary fiber has been elucidated.[13] Pentose polysaccharides, which occur in whole grains and vegetables and may contribute disproportionately to fecal bulk,[14] are suspected to play an important role.[15,16]

Vegetables and fruit may reduce the risk of colorectal cancer in several ways in addition to their dietary fiber content. The cruciferous vegetables (*Brassica cruciferae*), which include cabbage, broccoli, cauliflower, and Brussels sprouts, may be protective because of indoles that can stimulate production of liver microsomal enzymes capable of deactivating certain carcinogens.[17,18] Beta-carotene, which occurs in dark green and dark yellow-orange vegetables and fruits, may lower risk because, as an antioxidant, it may protect DNA and membrane lipids from oxidative degradation.[19] Also under investigation as inhibitors are vitamin C,[20,21] which is concentrated in certain vegetables and fruits, and the trace mineral selenium,[22,23] which is essential to the activity of the antioxidant enzyme glutathione peroxidase.

Recently, calcium has been suggested as a protective agent because of its capacity to convert ionized bile acids and fatty acids in the large bowel into insoluble calcium soaps that may be less irritating to colon epithelium.[24] Also, beer consumption has been proposed as a risk factor, particularly for rectal cancer,[25,26] but the findings have not been consistent.

Physical activity on the job has been linked to a reduced risk of colon cancer among males across several socioeconomic and ethnic groups.[27] A diet-related mechanism was suggested since physical activity is suspected to shorten fecal transit time and decrease

the churning of bowel contents. Sedentary occupations are correlated with obesity and weight gain, but these factors have been associated inconsistently with the risk of colorectal cancer.[28,29]

Evidence for the role of diet in the etiology of colorectal cancer has been reviewed by Zaridze[30] and Willett and MacMahon.[31] Insufficient research has been conducted to evaluate the importance of cruciferous vegetables, beta-carotene, vitamin C, selenium, or calcium. Of all the variables under consideration, a protective effect by dietary fiber has been the most consistently supported by epidemiologic studies, including both correlational and case–control investigations, although the evidence is not yet conclusive. Recent advances in understanding the role of fiber in colorectal cancer are discussed by Greenwald and Lanza[32] elsewhere in this book. Fat consumption has been implicated as a risk factor by geographic correlational studies, but the evidence from case–control studies has been inconsistent, perhaps because of the limited variation in fat intake among study populations in the United States and western Europe. Further, in some studies it has been difficult to distinguish between the effects of dietary fat, meat, calories, and total food intake, which are all being investigated.[33] Because the development of colorectal cancer is believed to be a multistep process involving initiation, promotion, and progression, and there is potential for inhibition at each step, several dietary components of a causative and protective nature may contribute to a person's risk of colorectal cancer.

A Preventable Disease ■

The epidemiology of colorectal cancer is of interest not only because of its high prevalence in the United States but also because risk may be radically altered within a person's lifetime by changes in life-style, presumably involving diet. This chapter reviews the epidemiologic evidence for this optimism, including the experience of migrant groups, and the recent patterns of colorectal cancer within the United States that may provide further clues to the causes and prevention of this cancer. For additional review of the epidemiology of colorectal cancer, we recommend Correa and Haenszel[28] and Schottenfeld and Winawer.[34]

If the risk of colorectal cancer can indeed be rapidly changed during a person's lifetime, it is likely that late stages rather than early stages of carcinogenesis are being accelerated or blocked. This mechanism and timing should increase opportunities for intervention strategies designed to prevent cancer.[35] Although much remains to be learned about the specific dietary components affecting the risk of colorectal cancer, there appears to be sufficient preliminary information to recommend a "prudent diet" that is low in fat and high in fiber (particularly since this kind of diet is likely to protect against other diseases common in western countries) and to anticipate that any lowering of the risk of colorectal cancer can be achieved by dietary modification in adult life.[36] The dietary hypotheses concerning colorectal cancer are under continued evaluation not only by the usual analytic approaches of epidemiology (case–control and cohort studies, some of which incorporate laboratory probes), but also by a series of intervention trials that alter diet during adult life by increasing fiber and decreasing fat intake or by supplementing the diet with such micronutrients as beta-carotene, vitamin C, and calcium.[37]

International Variation in Risk ■

Geographic Patterns ■

The incidence and mortality rates for colorectal cancer vary substantially around the world, indicating the importance of environmental factors, including those related to life-style. A comparison of incidence rather than mortality avoids intercountry differences in treatment and survival, although there may be some variation in diagnostic and reporting practices. Figure 10–1 summarizes the age-adjusted (world standard) incidence rates around 1975 for colon and rectal cancer by sex from the fourth edition of *Cancer Incidence in Five Continents*[38] and uses the same format as the third edition rates around 1970[39] presented by Correa and Haenszel.[28] For those countries with multiple registries or registries that include several ethnic groups, selected incidence data are included. The incidence rates for total colorectal cancer are emphasized because subdivision of the large bowel into colon and rectum may be somewhat arbitrary, and differences in classification and reporting may exist between countries. The geographic areas in Figure 10–1 are organized by continent to highlight the interregional variation that continues to exist for colorectal cancer.

Incidence rates for colorectal cancer are highest for both men and women in North America, Australia, and New Zealand. The Connecticut cancer registry reports the highest rate for males, 50 cases per 10^5 annually, and the second highest for females, 38 cases per 10^5. The rates in Atlanta, Georgia, located in the southern United States, are substantially lower than

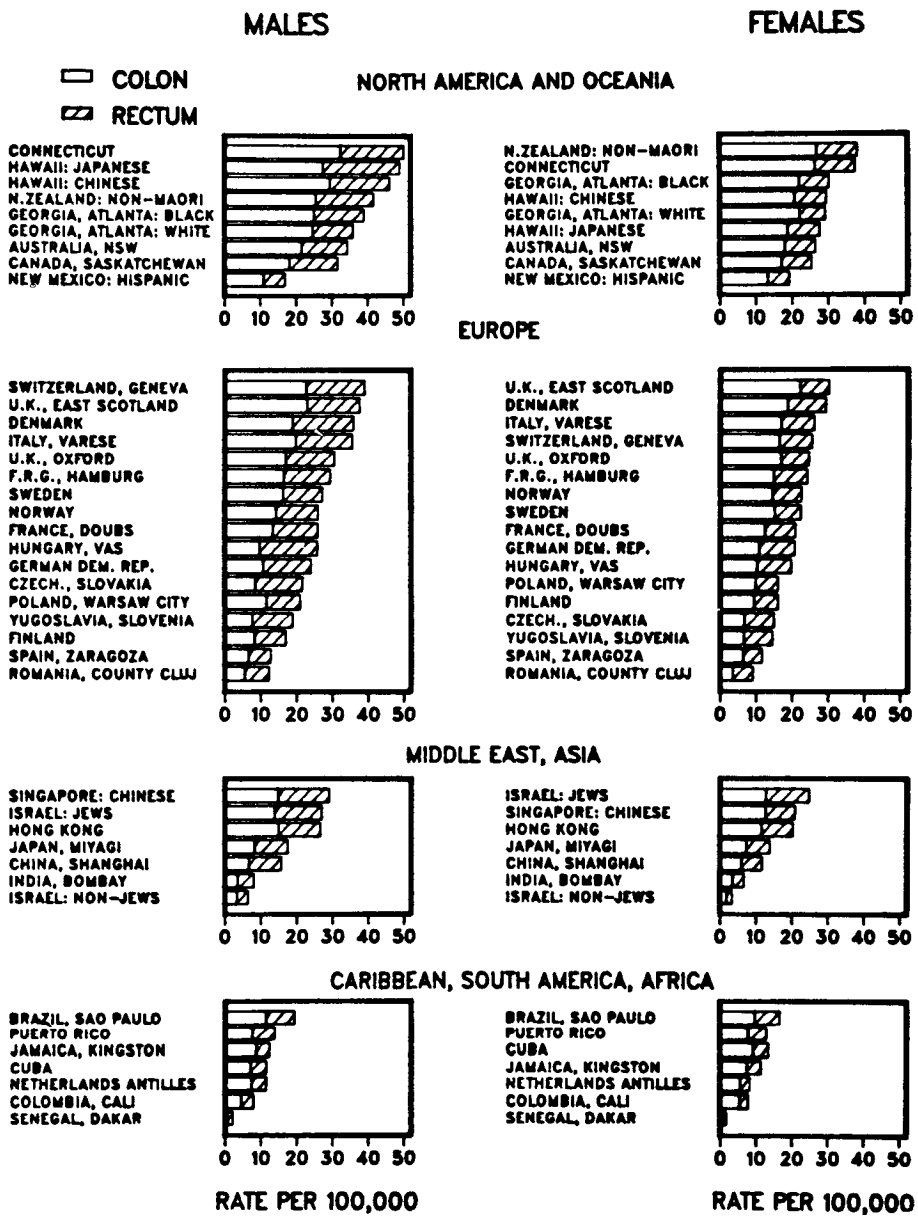


FIG. 10-1 Age-adjusted (world standard) incidence rates by sex for cancer of the colon and rectum, approximately 1975.[38]

the rates in Connecticut, representing the Northeast. The rates for colorectal cancer in Europe are generally lower than those in North America, Australia, or New Zealand, with the risk being consistently higher in western Europe than in eastern Europe. Incidence rates in Asia are variable with a relatively high risk, similar to western Europe, among the Jews of Israel, the Chinese of Singapore, and the people of Hong Kong, which are among the most westernized of Asian populations. The rates in Japan and the People's Republic of China (Shanghai), however, are intermediate, similar to eastern Europe, whereas Indians and the non-Jews in Israel have the lowest risks. The incidence rates in Latin American countries also vary, with rates in Colombia (Cali) as low as in India and with intermediate rates, similar to eastern Europe, in

Brazil (São Paulo). In the poorer, northeast sector of Brazil (Recife), however, rates are closer to those in Cali.[39] The lowest incidence among all the registries is in Senegal, the only African country included in the survey, with 2.1 cases per 10^5 annually for males and 1.7 per 10^5 for females. Although based on relatively few cases, these rates are 4% to 5% of those reported for Connecticut.

The male-to-female ratio in the incidence of colorectal cancer is not related to the rates of colorectal cancer in a given population. The recent international survey[38] revealed that males generally have a higher incidence than females, with the male-to-female ratio in nearly all the registries ranging from 1.1 to 1.4. The ratios were highest for the Japanese (1.8) and Chinese (1.6) in Hawaii, and lowest for the Hispanics in New Mexico (0.9) and for Cuba (0.9).

When Doll and Peto[3] attempted to calculate the proportion of cancer in the United States that is potentially avoidable, their estimates were based on the difference between the age-standardized incidence rates around 1970 for the United States and the lowest risk country with a reliable cancer registry.[39] Incidence rates were calculated for men and women under age 65, thus excluding the less dependable data for older persons. For both colon and rectal cancer in both sexes, the lowest risk was reported in Ibadan, Nigeria. Based on the variation in reported rates, about 90% of colon cancer in men and women in the United States was estimated as potentially avoidable, as was 85% of rectal cancer in men and 75% of rectal cancer in women. Similar estimates were derived when we used data from the more recent *Cancer Incidence in Five Continents* centered around 1975.[38] To temper the optimism inherent in these estimates, it should be emphasized that actual preventive measures await the positive identification of risk factors and that social and behavioral factors are likely to interfere with the adoption of certain measures that require changes in life-style.

Tumor Localization ■

The country-specific risks of colon and rectal cancer are highly correlated with one another, as shown for 39 registries in 33 countries in Figure 10–2; the correlation coefficient is greater than 0.85 for both males and females, based on a log–log scale. However, the incidence of colon cancer varies internationally to a greater extent than does that of rectal cancer. In many countries with low rates for colorectal cancer such as Senegal, India, and Rumania, the incidence of colon cancer is less than that of rectal cancer. As the risk

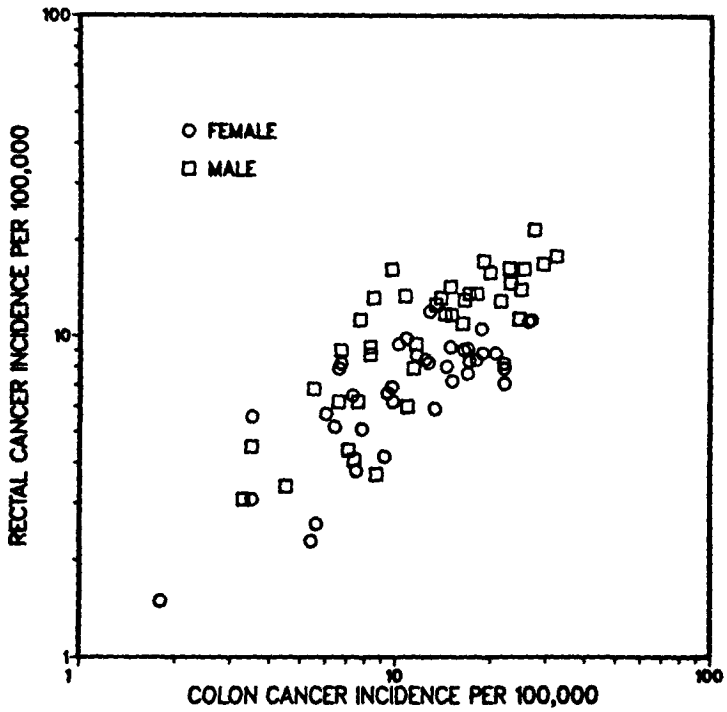


FIG. 10–2 Correlation of age-adjusted (world standard) incidence rates by sex for cancer of the colon and rectum, approximately 1975: 39 registries.[38]

of colorectal cancer rises, however, colon cancer becomes more frequent than rectal cancer so that in Connecticut, colon cancer is 1.8 times as common as rectal cancer among men and 2.4 times as common among women.

De Jong and colleagues[40] examined the distribution of colorectal cancer by anatomic region in countries with varying risk of this disease. Based on incidence data from 12 countries, the subsite distribution appeared similar in countries with high and intermediate risks, but a deficit of sigmoid cancers seemed to characterize low-risk countries. Cancers in the rectosigmoid, however, were not classified consistently by different countries, although this did not appear to have a large effect on the overall patterns. Berg and Haenszel attempted to collect more accurate data to clarify this issue.[28] In six populations drawn from the extremes of colorectal cancer incidence, relatively objective measurements were made of the distance of the malignancy from the anus, using sigmoidoscopy whenever possible. In Cali, Colombia, a low-risk population, cancer incidence for both sexes was distributed more uniformly along segments of the bowel than in Iowa, a high-risk population. In Iowa the per centimeter incidence of tumors was highest in both sexes for the segment 6 to 15 cm from the anus, which comprises both the upper rectum and the rectosigmoid. The subsite distribution, however, was not proportional in the two countries, and the segments displaying the largest incidence ratio for Iowa relative to Cali were the descending colon and the sigmoid colon ≥16 cm from the anus.

Migrant Studies ■

Although some of the international variation of colorectal cancer may have a genetic basis, evidence supporting a major role for environmental and lifestyle factors can be found in studies of migrant populations. In general, as groups of people move to a new land, their risk of various cancers shifts away from the pattern prevailing in the country of origin toward that of the host country.[41] General environmental exposures, such as water quality, sunlight, or air pollution, are altered immediately on arrival in the host country for all groups of migrants. Life-style practices, such as dietary patterns, alcohol and tobacco use, sanitary habits, or sexual and reproductive practices, may change slowly, however, perhaps over several generations, and the speed and extent of acculturation may vary by ethnic group.

Migrants to the United States ■

Lilienfeld and colleagues[42] analyzed for U.S. whites the variation in site-specific cancer mortality by country of birth during 1959–1961 and compared the rates to those in the countries of origin during 1960. Figure 10–3 shows the age-adjusted (1950 U.S. standard) mortality rates for intestinal (colon and small intestine) and rectal cancers, as well as, for comparison, stomach cancer. Stomach cancer rates in virtually all the countries shown were higher than in the United States; rates among those who had migrated to the United States were generally lower than those in the country of origin but higher than those for U.S.-born whites. In contrast, colorectal cancer mortality rates in most other countries were lower than those in the United States; however, the rates among migrants not only approached those of the U.S. native-born whites but also exceeded them in many instances. The differences between the rates in the countries of origin and those in the United States were considerably greater for stomach cancer than for colorectal cancer; this may have contributed to the greater convergence of colorectal cancer rates among the foreign-born toward the rates of U.S. native-born whites. Not all migrant groups, however, acquired the U.S. risk in the first generation. Those born in Mexico retained colorectal cancer rates that were about 50% those of native-born white Americans. In addition, colorectal cancer mortality rates among the foreign-born did not reach U.S. rates as frequently for women as for men. When the mortality rates among the U.S. foreign-born were compared with those in the countries of origin for other primary sites, the rates among the foreign-born for breast, corpus uteri, and prostate cancer were also more closely aligned with those for U.S. native-born whites. This pattern suggests that the risks for these cancers changed within the lifetime of the migrants to resemble the prevailing U.S. risks. Haenszel[43] surveyed the mortality of foreign-born and native U.S. whites by country of origin in 1950 and generally reached the same conclusions, although suitable comparisons could not be made with rates in the countries of origin because only limited international mortality data were available.[44]

A mortality survey of Japanese-Americans (both native- and foreign-born) during 1949–1952 revealed that the rates for colon and rectal cancer among U.S. Japanese were lower than among U.S. whites, and higher than among Japanese in Japan.[45] This upward shift was particularly apparent in males. A decade later, when Haenszel and Kurihara[46] reported the re-

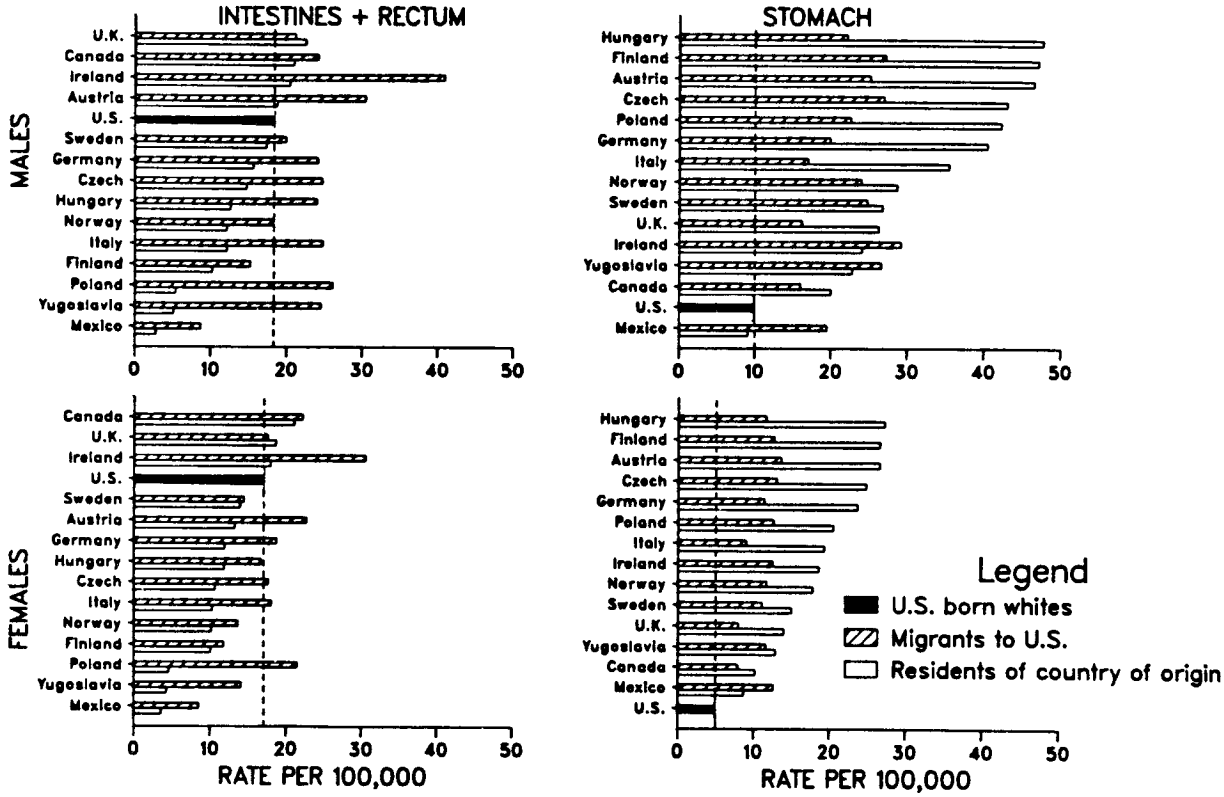


FIG. 10–3 Age-adjusted (1950 U.S. standard) cancer mortality rates for migrants to the United States from selected countries, 1959–1961; residents of the countries of origin, 1960; and U.S.-born whites, 1959–1961.[42]

sults for 1959–1962, colon and rectal cancer mortality rates for Japanese-Americans moved even closer to U.S. white rates (Table 10–1). Over time, the average number of years of U.S. residence had increased for Japanese-Americans, and more were Nisei (children of migrants) than Issei (the migrants themselves). These trends have continued, so that by the period 1968–1972, colon cancer incidence rates for Japanese men and women in Hawaii were similar to those for whites in Hawaii up to age 70 (mostly Nisei) but were still lower for ages over 70 (mostly Issei).[28]

An autopsy survey of elderly Japanese patients in Hawaii revealed small asymptomatic colorectal cancers in 3.4% of the subjects.[47] This observation and others prompted Correa and Haenszel[28] to suggest that the increasing risk of colorectal cancer in mi-

Table 10–1
Standardized Mortality Ratios for Cancer of the Colon and Rectum in U.S. Japanese, Relative to U.S. Whites and to Japan

		Colon		Rectum	
SMRs for U.S. Japanese	Year	Male	Female	Male	Female
Relative to U.S. whites	1949–52	0.67	0.34	0.80	0.65
	1959–62	0.70	0.46	0.95	0.63
Relative to Japan	1949–52	3.71	1.74	1.37	0.91
	1959–62	3.46	2.11	1.34	0.69

Haenszel W, Kurihara M: Studies of Japanese migrants: I. Mortality from cancer and other diseases among Japanese in the United States. JNCI 40:43–68, 1968.

grants may be initially expressed as small neoplasms among older males. The cancers among migrants preferentially affected the sigmoid colon and were paralleled by an increased risk of premalignant adenomatous polyps.

The Japanese experience indicates that colon and rectal cancer mortality rates have risen toward American rates in the migrating generation, but as yet the transition is not as complete as in most of the European migrant groups.[48] Although mortality from colon and rectal cancer in the Issei was intermediate between levels in Japan and in the United States, the mortality rates for stomach and breast cancer among the Issei remained close to those of Japan. As colon and rectum cancer rates in the Nissei continued to rise toward the prevailing U.S. rates, stomach cancer rates started to fall while breast cancer rates showed little change.[46] Therefore, of these three cancers, risk of colorectal cancer was influenced the most rapidly by migration to the United States.

Analytic studies of colorectal cancer have been carried out among the Hawaiian Japanese to exploit the variability in dietary patterns and risk of disease. The first, a case–control study with hospital controls, found that meats (especially beef), legumes (especially string beans), and starches were consumed more frequently among the cases,[49] whereas no such associations were seen in a parallel study in three prefectures of Japan.[50] Neither study formed estimates of total fat, but meat and fat consumption were assumed to be highly correlated. More recently, a cohort study among Hawaiian Japanese found no evidence of a positive relation between colon cancer and the intake of total fat or saturated fat, expressed as absolute values or as a percentage of caloric intake.[51] Thus the two studies of colorectal cancer among the Hawaiian-Japanese are inconsistent with respect to the role of dietary fat, and the influence of dietary fiber has not been assessed. Fecal mutagens have been found more frequently among Hawaiian Japanese than in a low-risk population from a rural area of Japan.[52]

Attention has also centered on the risks of cancer among Chinese-Americans. Until recently, however, mortality statistics were unavailable for the People's Republic of China. In China the geographic variation in cancer risk is striking, and not all cohorts of migrants to the West have originated from the same regions of China. In the early 1960s the standardized mortality ratios (SMRs) among men and women in Hong Kong, Singapore, and Taiwan, relative to U.S. whites, were between 0.3 and 0.5 for colon cancer, and between 0.6 and 0.9 for rectal cancer.[53] Fraumeni and Mason[54] examined the cancer mortality experience of Chinese-Americans for 1950–1969 and noted that colon and rectal cancer mortality among Chinese males slightly exceeded that for U.S. white males (age-adjusted mortality rate ratio = 1.1–1.2), whereas among Chinese females the rates increased, but did not reach the level for U.S. white females (0.5–0.6). Two other analyses of Chinese-American mortality covering 1959–1962 and 1968–1972[53,55] revealed that colon and rectal cancer mortality among foreign-born Chinese approximated U.S. rates more closely than did mortality for breast or stomach cancer.

Recently the changing mortality patterns among Chinese migrants have been reviewed in light of the 1975 National Mortality Survey in the People's Republic of China.[56] The majority of Chinese entering the United States have come from Guangzhou province and are identified by their Cantonese dialect. Around 1970 age-adjusted mortality rates of colorectal cancer among foreign-born Chinese-American men and women were 5.6 and 2.7 times the respective rates in Guangzhou province. The sharp increase in risk of colorectal cancer on migration to the United States is accentuated by using for comparison the rates from Guangzhou rather than from Hong Kong, where the risks are about three times those in Guangzhou even though the people of Hong Kong are mainly Cantonese. Colorectal cancer mortality among the U.S.-born Chinese-Americans, relative to foreign-born Chinese, continued to rise for women but dropped for men, an anomaly also noted in the earlier studies.[53,55]

The descriptive epidemiology of cancer in Chinese populations has been pursued only recently by analytic studies in the United States, in contrast to the extensive research that has been conducted on Japanese-Americans[57]; however, the active collaboration now underway between cancer epidemiologists in the United States and the People's Republic of China is stimulating many investigations, including collaborative case–control studies of colorectal cancer among Chinese in both countries.

Another set of migrants to the United States, the Puerto Ricans, are of interest in two respects. The vast majority came after World War II, unlike the Europeans and Japanese. In addition, they frequently travel back and forth between the mainland and Puerto Rico, so that their exposures on the mainland are intermittent and of variable duration. Reverse migration is so common that in the 1970s the net flow was in the direction of migrants returning to Puerto Rico.[58] Monk and Warshauer[59] examined age-adjusted colon cancer mortality rates between 1958 and 1971 for migrants born in Puerto Rico and living in New York City and for all other whites in New York City. Colon cancer mortality in New York,

compared to Puerto Rico, was five times higher among white men and three times higher among women. Puerto Rican-born men living in New York showed only a small increase in colon cancer mortality, with rates 1.5 times those in Puerto Rico, whereas Puerto Rican-born women in New York showed an even smaller increase. Most Puerto Rican migrants, however, may not have reached an age when elevated risks of colon cancer would become apparent, so that the New York Puerto Rican rates are based on small numbers of deaths. Recently, Warshauer and co-workers[58] examined age-adjusted incidence and mortality rates for colorectal cancer among Puerto Rican-born residents of New York City for 1975–1979. Their rates have moved closer to the rates for other New York whites. Incidence and mortality for Puerto Rican men and women living in New York were about twice the rates reported in Puerto Rico and one half to two thirds the rates of other New York whites. Thus, Puerto Ricans have experienced in the migrating generation an increase of colon cancer but not to the same extent as have European migrants to the United States.

Migrants to Australia and Israel ■

Like the United States, Australia has attracted many migrants from western and eastern Europe. Unlike the United States, most migrants to Australia arrived after World War II. The young and middle-aged adults who came to Australia during the 1950s are now reaching the age at which cancer is common. McMichael and associates[60] calculated age- and sex-standardized cancer mortality ratios for migrants by country of origin and duration of residence in Australia, relative to the Australian-born population, for several gastrointestinal cancers during 1962–1976 (Table 10–2). By comparing migrants from a particular country who resided in Australia for different periods of time, it was possible to evaluate a suspected bias, namely, that the risk of a migrant group may reflect the experience of a nonrepresentative, self-selected population in the country of origin. The four "continental European" migrant groups (from Poland, Yugoslavia, Greece, and Italy) whose native risks of colon cancer ranged from 0.3 to 0.7 of that in Australia, showed an increased risk of colon cancer with increasing duration of stay. However, colon cancer mortality rates among the migrating populations from Yugoslavia, Greece, and Italy have not reached the rates of native-born Australians; only rates among the Polish migrants have risen to Australian rates. By contrast, Scottish migrants, with an initially high risk of colon cancer, experienced a declining risk with increasing years in Australia. Rectal cancer in "continental European" migrants showed even larger relative increases than colon cancer, although for Greek and Italian migrants the rates did not reach those of native Australians in the migrating generation. In British migrants there was a marked decline toward the risk of rectal cancer among native Australians. Among the "continental European" migrants, the increase in risk of colon cancer, and to a lesser extent rectal cancer, was greater in men than in women.

Table 10–2
Age- and Sex-Standardized Mortality Ratios During 1962–1976 for Cancer of the Colon and Rectum in Migrants to Australia, Relative to Native-Born Australians, by Duration of Residence

Country of Origin	Colon Years in Australia		Rectum Years in Australia	
	≤16	>16	≤16	>16
England	0.99 (497)*	1.04 (2327)	1.23 (214)	1.04 (800)
Scotland	1.47 (126)	1.24 (675)	1.05 (33)	1.08 (216)
Ireland	0.62 (26)	1.06† (218)	1.17 (13)	1.18 (90)
Poland	1.02 (33)	1.14 (106)	0.43 (15)	1.34† (40)
Yugoslavia	0.47 (21)	0.66 (37)	0.46 (14)	1.34† (22)
Greece	0.36 (24)	0.69† (58)	0.34 (11)	0.70† (24)
Italy	0.37 (65)	0.70† (183)	0.48 (31)	0.80† (80)

McMichael AJ, McCall MG, Hartshorne JM, Woodings TL: Patterns of gastrointestinal cancer in European migrants to Australia: The role of dietary change. Int J Cancer 25:431–437, 1980.

* Numbers of deaths among migrants are in parentheses.

† Differs from mortality ratio for ≤16 years, $p < 0.05$.

A high proportion of the adult Chinese living in the Australian state of New South Wales (NSW) was born elsewhere, most commonly in China, where the rates of colorectal cancer are relatively low for both sexes. Zhang and co-workers[61] noted that among the NSW migrants born in China, males acquired a higher mortality from colorectal cancer than did Australian-born NSW residents (SMR = 2.0), whereas females moved upward but did not reach native Australian rates (SMR = 0.7). Although the SMRs are based on relatively few deaths, this trend parallels what was seen among Chinese-Americans.

Of interest, Scottish and British migrants to Australia have shown a decline in the risk of colon and rectal cancer, respectively, corresponding to migration from a higher to a lower risk area. Israel is another country where some migrants may be experiencing a decrease in risk. Based on age-adjusted incidence rates for 1973–1977,[38] Israeli-born Jews had a risk of colon and rectal cancer below that of Israelis born in Europe or America and above that of Israelis born in Africa or Asia (Table 10–3). The incidence rates were closer to the European-American levels among Israeli-born

males than among females. Earlier incidence data from 1968–1972[39] also showed an intermediate level for colon and rectal cancer among the Israeli-born, except that the rates for both sexes were closer to those of the African- or Asian-born Israelis than to those of the European- or American-born Israelis; however, without knowing the precise heritage of the Israeli-born Jews, the evidence that some have experienced a decline in the risk of colorectal cancer compared to their parents is suggestive but not conclusive.

Implications of Migrant Studies ■

Several conclusions can be drawn from studies of colorectal cancer in migrating populations.

1. The risk of colon and rectal cancer can change in the migrating generation and, as seen in the European migrants to the United States, closely approach that of the country of destination. The effects appear real and not related to selective factors or other biases. In studies of Japanese migrants, the effects varied by segment of the colon, with an elevated risk first appearing in the sigmoid region. In view of the gathering evidence linking diet to colorectal cancer, it appears that changes in dietary patterns may contribute to the modification of risk within 2 to 3 decades.
2. The risk of colon and rectal cancer seems to change more rapidly in the migrating generation than does the risk of other major cancers. Two explanations are possible: The risk of colorectal cancer may be determined primarily by adult diet, whereas the risk of other cancers such as stomach and breast is more influenced by exposures earlier in life; or dietary factors and mechanisms related to colorectal cancer change more rapidly with acculturation than do the determinants of other cancers.
3. The risk of colorectal cancer can be radically altered in the migrating generation, but it need not be. Although European migrants to the United States experienced a transition to native-born risks in the first generation, the Japanese, Mexican, and Puerto Rican migrants did not. Not all nationalities who migrated to Australia acquired native-born Australian rates in the first generation. The extent of acculturation and the choice of life-style and diet appear to be crucial.
4. The rates of colorectal cancer often rise on migration simply because the risks are higher in the country of destination than in the country of origin. The risk of colorectal can also decline with migration. Scottish and British migrants to Australia experienced a decline in risk of colon and rectal cancer, respectively. A reduction in risk may also be occurring among European-American migrants to Israel, although the data are not conclusive.
5. In migrant studies the mortality from colorectal cancer seems to rise more quickly among men than women. This sex difference in colorectal cancer mortality was observed in European, Japanese, Chinese, and Puerto Rican migrants to the United States and in "continental European" migrants to Australia. Either males more readily adopt the pertinent dietary patterns or are more susceptible to carcinogenic events. It is unclear whether males also experience a more rapid decline in colorectal cancer on migration to a country with lower risk. Male migrants to Australia from Scotland and England have shown a greater decrease in colon and rectal cancer, respectively, than have females. Israeli-born females of European-American ancestry, however, seemed to experience a greater decrease in colorectal cancer than did males.
6. Migrant populations provide an exceptional opportunity for analytic studies to exploit the diversity of dietary patterns and other aspects of life-

Table 10–3
Age-Adjusted (World Standard) Incidence (per 100,000) of Colon and Rectal Cancer in Israel for 1973–1977 by Religion and Place of Birth

	Males		Females	
Israeli Population	Colon	Rectum	Colon	Rectum
Jews born in Europe or America	14.5	13.9	14.4	13.4
Jews born in Africa or Asia	6.8	5.7	5.5	4.6
Jews born in Israel	13.6	11.7	10.0	9.5
Non-Jews	3.3	3.1	1.8	1.5

Waterhouse J, Shanmugaratnam K, Mair C, Powell J (eds): Cancer Incidence in Five Continents, vol IV. IARC Scientific publ no 42. Lyon, France, International Agency for Research on Cancer, 1982.

style and to identify the factors responsible for the changing risks of colorectal cancer as well as precursor lesions, notably polyps.

A recent review of migrant studies[41] suggested that attention is shifting from the United States to other countries such as Australia, Canada, Brazil, and Israel where substantial numbers of migrants arrived after World War II; however, the recent influx of migrants into the United States from Mexico, Puerto Rico, Cuba, and other Latin American countries and from Southeast Asia may provide new opportunities for study as these populations reach the ages when cancer becomes more common.

Recent Patterns in the United States ■

In the United States, the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute (NCI) supports and coordinates several population-based cancer registries in selected cities and states, which provide incidence, mortality, and survival data for more than 10% of the U.S. population.[62] Recent data from the SEER program for 1978–1981 indicate that the average annual age-adjusted (1970 U.S. standard) incidence rates for both colon and rectal cancer are higher among males (39.0 and 19.2 per 10^5) than among females (32.0 and 11.8 per 10^5).[63] Nonetheless, in 1985 more cancers of the colon (52,000 compared to 44,000) and only slightly fewer cancers of the rectum (20,000 compared to 22,000) were diagnosed among females than among males.[1] This apparent discrepancy arises from the larger proportion of women in the older age groups, which are at higher risk of developing cancer.

Time Trends ■

The SEER program began in 1973, but incidence data from five geographic areas (Atlanta, Detroit, San Francisco, Iowa, and Connecticut) are available from the late 1940s and can be pooled to assess the secular trends in cancer incidence among U.S. whites.[64] The NCI conducted surveys in the first four areas during different years between 1947 and 1950[65,66] and in 1969–1971,[67] while the cancer registry in the state of Connecticut has provided continuous data since the late 1930s.[68] From the late 1940s to 1979–1980 the age-adjusted (1970 U.S. standard) incidence of colorectal cancer among white males increased more than 30%, whereas among white females the incidence changed little between the late 1940s and 1970 but has increased during the past decade (Fig. 10–4). The upward trend in both sexes has been restricted to cancers arising in the colon. Since the late 1940s the incidence rates for rectal cancer have remained fairly stable. In comparison, mortality rates for colorectal cancer in the United States have remained level among white males and have declined about 27% among white females (Fig. 10–4), reflecting improvements in survival. The mortality rates for colorectal cancer in the five geographic areas combined have remained slightly higher than in the total United States, but the trends have been quite similar. The sex-related divergence over time in both incidence and mortality rates for males and females has resulted in the male-to-female *incidence* ratio increasing from 1.07 to 1.35 and the male-to-female *mortality* ratio (for the United States) increasing from 1.04 to 1.39 over the last 30 years.

The incidence trends for colorectal cancer have differed according to age (Figs. 10–5, 10–6). Among

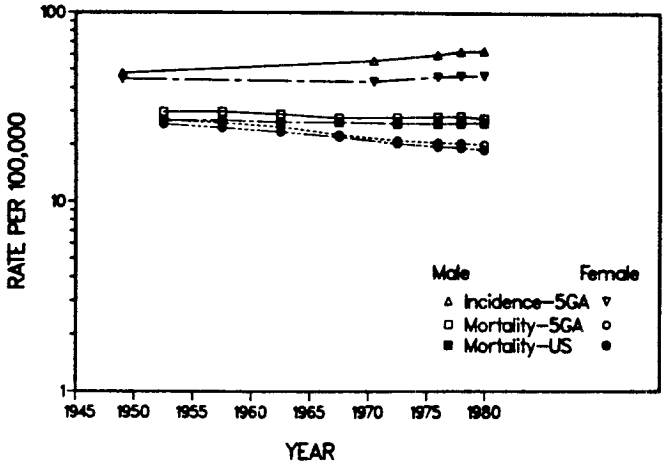


FIG. 10–4 Age-adjusted (1970 U.S. standard) incidence and mortality trends for colorectal cancer among whites.

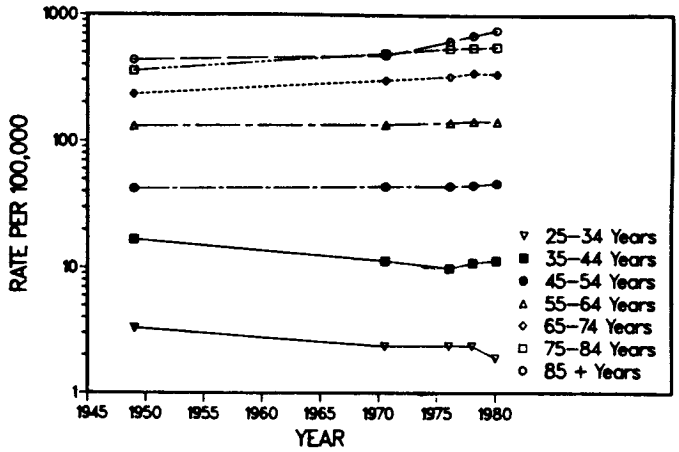


FIG. 10–5 Age-specific colorectal cancer incidence trends among white males in the five U.S. geographic areas.

white males and females, incidence declined in the younger age groups (<45 years), primarily between the late 1940s and 1970, but increased at older ages (≥65 years). The decreases at younger ages were proportionately greater among females than males (about 50% compared to 30–40%). Similarly, the increases at older ages were proportionately smaller among females than males (14%, 20%, and 63% compared to 44%, 56%, and 74% for the age groups 65–74, 75–84, and 85+, respectively). The substantial rise in incidence at 85+ years may be related in part to improved diagnosis in the elderly or a shift toward an older population with higher risks.

Figure 10–7 shows the recent age-adjusted (1970 U.S. standard) incidence trends by subsite for white males and females using a linear rather than logarithmic scale (*cf.* preceding figures). For both sexes, incidence rates have increased for the ascending and transverse colon, especially the former, but have remained relatively stable for the descending colon. The rates have also increased for the sigmoid colon and rectosigmoid but have decreased for the rectum. It is difficult to determine whether this change results from a more accurate localization of rectosigmoid cancers previously assigned to the rectum. The reporting of colorectal cancers without specification of subsite was relatively low in both sexes for the decade and decreased only slightly, indicating that subsite trends do not reflect more detailed coding. These trends represent an extension of earlier observations in Connecticut, which showed increases of colon cancer since 1940, especially affecting ascending and sigmoid segments of the colon.[69]

The trends by subsite have implications not only to etiology but also to early cancer detection. Among white males and females the highest number of colorectal tumors are currently located in the ascending colon (22% in men, 27% in women) and the sigmoid colon (25% and 23%, respectively). Progressively fewer tumors are found in the rectum (22% in men, 16%

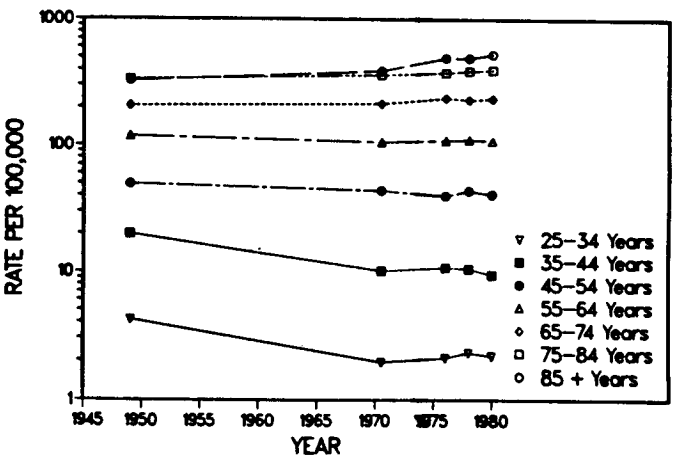


FIG. 10–6 Age-specific colorectal cancer incidence trends among white females in the five U.S. geographic areas.

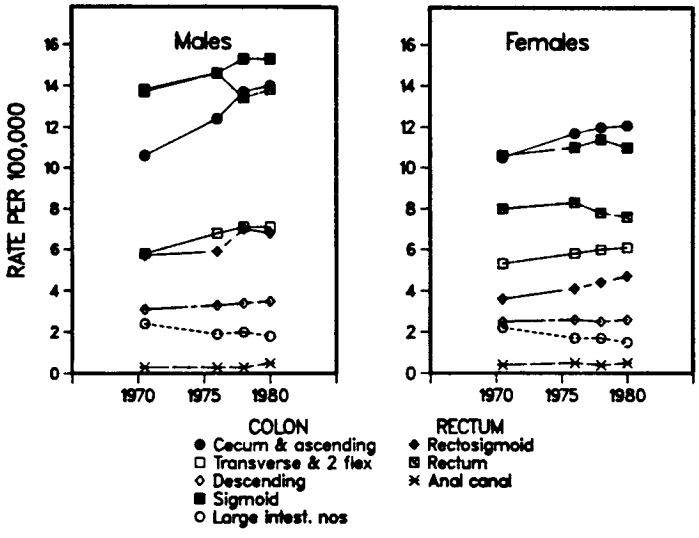


FIG. 10–7 Site-specific age-adjusted (1970 U.S. standard) colorectal cancer incidence trends in the five U.S. geographic areas among whites.

in women), transverse colon (11% and 13%, respectively), rectosigmoid (11% and 10%, respectively), and descending colon (6% and 6%, respectively). Because of the increasing percentage of tumors in the ascending colon, a smaller percentage of colorectal cancer would have been detected in 1980 than in 1970 by rigid or flexible proctosigmoidoscopic examinations. Assuming that the rigid scope covers half the rectosigmoid region, 29% of the colorectal cancers in men and 23% in women would have been visible in 1980, compared to 32% and 25% in 1970. Assuming that the flexible scope expands vision through the sigmoid colon, 60% of the colorectal cancers in men and 52% in women would have been visible in 1980, compared to 63% and 55% in 1970.

Race and Ethnicity ■

The incidence of colorectal cancer has risen sharply over time among U.S. blacks to approximate the risks currently experienced by the white population. Between 1937–1939 and 1969–1971 the incidence of colorectal cancer in nonwhites (primarily blacks) increased 84% in men and 94% in women, whereas the incidence increased only 19% in white men and decreased 4% in white women.[70] Figures 10–8 and 10–9 show recent (1978–81) age-specific incidence and mortality rates for colorectal cancer in black and white men and women. The risk of colorectal cancer increases exponentially with age, except at the oldest age group. Among whites the incidence and mortality

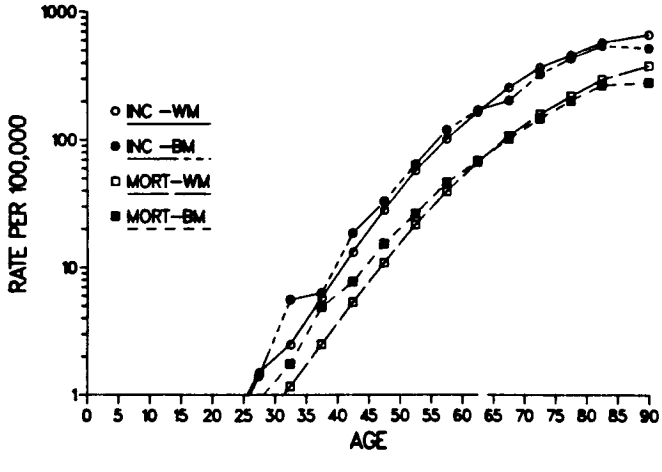


FIG. 10–8 Age-specific SEER incidence rates and U.S. mortality rates for colorectal cancer among white and black males: 1978–1981.[63]

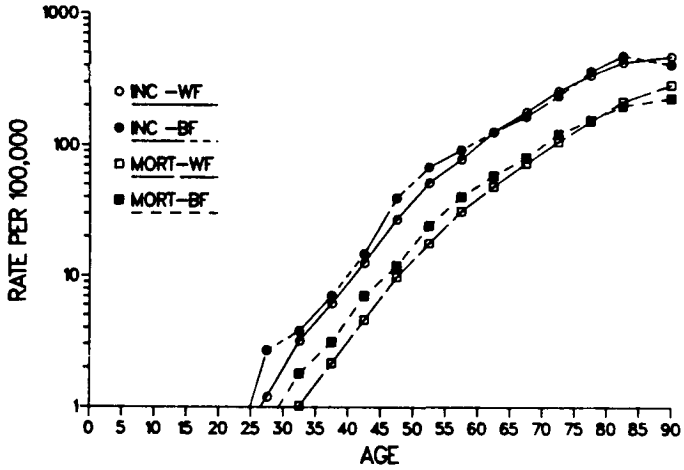


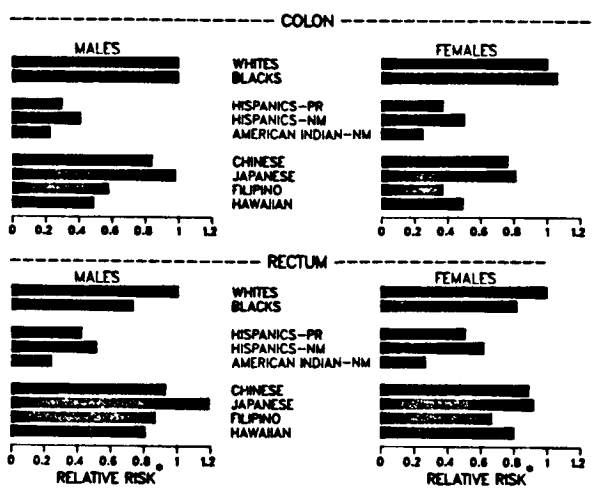
FIG. 10-9 Age-specific SEER incidence rates and U.S. mortality rates for colorectal cancer among white and black females, 1978–1981.[63]

curves for each sex are roughly parallel, suggesting similar survival at most ages. Of note, the incidence of colorectal cancer under age 60 is higher among blacks than whites, while at the older ages the incidence is generally higher among whites. Mortality rates are also higher among blacks than whites before age 65 for males and before age 80 for females. This elevated risk of colorectal cancer among blacks at the younger ages suggests that the recent observed increases are real, with successive cohorts of blacks experiencing higher risks of colorectal cancer. If improved diagnosis were responsible for the increased rates in blacks, the older age groups would be primarily affected. Although the responsible risk factors are uncertain, a diet low in fiber and high in saturated fat was implicated in a case–control study of colorectal cancer among U.S. blacks.[71]

SEER data for the years 1973 to 1981 were combined to maximize the numbers of cases available for analysis of racial and ethnic variation (Fig. 10–10). For blacks the overall risk of colon cancer among males has reached the level for whites, whereas the risk among females has surpassed it (relative risk [RR] = 1.1); however, rectal cancer in blacks is still less common than in whites for both sexes (RR = 0.7–0.8). Hispanics have a substantially lower incidence of colon and rectal cancer than do whites for both sexes (RR = 0.4–0.6 in New Mexico and 0.3–0.5 in Puerto Rico), whereas American Indians in New Mexico have the lowest risks of all (RR = 0.2–0.3). Japanese females and Chinese of both sexes have rates of colon and rectal cancer 0.8 to 0.9 those of whites, but Japanese males have risks of colon cancer equal to whites (RR = 1.0) and of rectal cancer higher than whites (RR = 1.2). The rates for Filipinos and native Hawaiians generally are below those of the Chinese and Japanese but above those of the Hispanic groups.

Among the Chinese, Japanese, and Filipino populations, the risks of colon and rectal cancer among males are closer than among females to the rates in the white population. Among the black, Hispanic, and American Indian populations, however, the risks at both sites among females tend to be closer than among males to the rates in the white population. In general, the risk of colon cancer tends to vary more than the risk of rectal cancer. In all the ethnic/racial groups except blacks and Japanese males, the risks of

FIG. 10-10 Racial/ethnic variation in incidence of colon and rectal cancer: SEER, 1973–1981. PR = Puerto Rico; NM = New Mexico.* All risks are expressed relative to the risk among whites, based on age-adjusted rates (1970 U.S. standard).



rectal cancer are closer to those of whites than are the risks of colon cancer.

The risks among the Japanese, Chinese, and Filipinos reflect the proportion of foreign-born and native-born in the San Francisco-Oakland and Hawaii registries. In the states of California and Hawaii combined (appropriate data are not readily available for San Francisco-Oakland alone) in 1980, 20% of the Japanese, 56% of the Chinese, and 62% of the Filipinos were foreign-born.[72] Although incidence data from the SEER program (1973–81) indicate that the colorectal cancer rate among Chinese men was somewhat lower than that among U.S. whites, earlier mortality rates among Chinese-American males for 1950–1969 slightly exceeded that for U.S. whites.[54] One explanation may be poor survival among Chinese-Americans, but another may be the heavy influx of Chinese into the United States since the repeal of the National Origins Quota Act in 1965.[73]

Urbanization and Socioeconomic Status ■

In countries at high, intermediate, and low risk of colorectal cancer, the rates are consistently higher among urban residents.[28] Incidence data around 1950 for New York State, Connecticut, and Iowa suggested that the urban excess was more prominent for men than for women, and for colon than for rectal cancer.[74] U.S. mortality data for 1949–1951 showed that an excess risk of colorectal cancer in metropolitan versus nonmetropolitan counties existed in all regions of the country.[75] Detailed residential histories for a sample of the U.S. population who died of colorectal cancer in 1958 were used by Haenszel and Dawson[75] to show that long-term male and female residents (>40 years) of urban counties had SMRs for colorectal cancer of 1.1 and 1.2, respectively, whereas long-term male and female residents of rural counties had SMRs of 0.5 and 0.7 (all SMRs calculated relative to U.S. white males and females, age 35+). Since the urban excess was enhanced by comparing long-term rather than current residents, it could not be attributed to patients coming to major cities for medical care. It was also observed that current residence in an urban or rural area was a stronger determinant of risk of colorectal cancer than was place of birth (Table 10–4). The risk for persons born in rural areas and migrating to large cities resembled that for persons born and currently residing in large cities. Conversely, the risk for persons moving to rural areas from large cities resembled that for persons born and residing in rural areas. This provides further evidence that the risk of colorectal cancer is influenced more by comparatively recent events than by remote exposures of early life, which is consistent with the experience of foreign-born migrants to the United States.

Table 10–4
Standardized Mortality Ratios for Colorectal Cancer by Birthplace and Current Residence, Relative to U.S. White Males and Females: 1958

	Birthplace			
	Males		Females	
Current Residence	Urban	Rural	Urban	Rural
Urban	0.98	0.95	1.12	1.10
Rural	0.85	0.69	0.71	0.67

Haenszel W, Dawson EA: A note on mortality from cancer of the colon and rectum in the United States. Cancer 18:265–272, 1965.

By 1970 incidence data for Iowa and Colorado indicated that an excess risk in urban areas occurred only for colon cancer among males, with no gradient apparent for female colon cancer or rectal cancer in either sex.[76] Urban–rural gradients in both incidence[76] and mortality[77] from colorectal cancer appear to have diminished in the United States over time.

No clear socioeconomic gradient in risk of colon or rectal cancer was noted for either sex in the 1947–1948 cancer incidence survey of ten metropolitan areas, which classified census tracts by median family income.[65] In a study of colon and rectal cancer mortality among U.S. whites during 1950–1969 by county, however, Blot and colleagues[78] observed positive correlations for both sexes with county income and (to a lesser extent) median years of education. The elevated risk with increasing socioeconomic status was seen in all regions and in counties with both large (≥75,000) and small populations. Better medical care and survival among the more affluent would tend to diminish rather than inflate the higher risks reported among the upper socioeconomic classes.

Devesa and Diamond[79,80] have combined data from the urban areas of the Third National Cancer Survey (1969–71) with 1970 census data to assess the relationship of cancer incidence to socioeconomic status. Median years of education and median family income by census tract of residence at the time of diagnosis were used as indicators. Only in white males was the risk of colorectal cancer associated with socioeconomic status, and the associations with colon and rectal cancer were in different directions (Fig. 10–11). Significant positive associations with both income and education were apparent for colon cancer among white males; the risks in the highest income

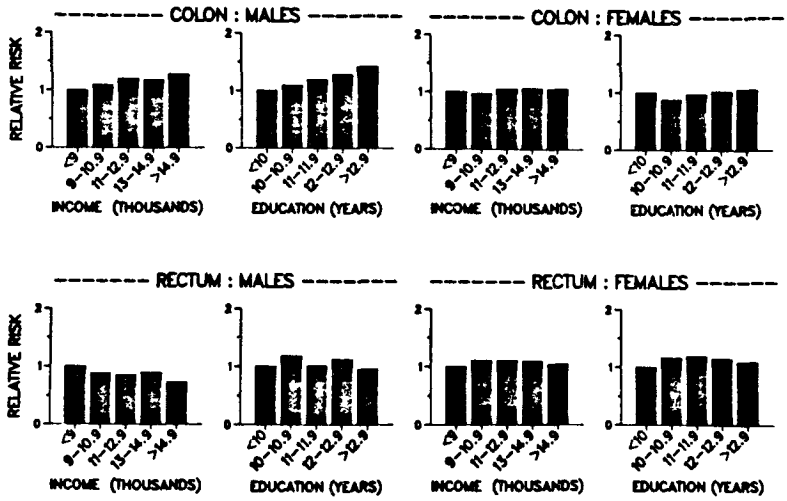


FIG. 10-11 Association of socioeconomic variables and incidence of colorectal cancer among whites: TNCS, 1969–1971. Risks are expressed relative to the risk in the lowest income or education category and are based on rates adjusted for age and geographic area.

and education groups were, respectively, 1.3 and 1.4 times those in the lowest groups. Among white females only the barest suggestion of a positive association with either measure was apparent. On the other hand, rectal cancer showed a significant inverse association with income among white males, with the highest income category having a risk 0.7 times that of the lowest; education, however, did not exert a consistent influence on risk. Neither income nor education was associated with the risk of rectal cancer among white females. Consistent patterns were not apparent for either site among blacks in the study. In the United States and in other developed countries, socioeconomic status does not seem to be as strongly associated with colorectal cancer risk as does urbanization.[28]

Religion ■

Newill[81] investigated patterns of cancer mortality among New York City whites of different religions during 1953–1958, basing religious affiliation on choice of funeral home and cemetery. Jewish males and females, respectively, had 1.37 and 1.24 times the colon cancer risk of Catholics and Protestants, who had similar rates. Risk of rectal cancer was not influenced by religion. Subsequent studies on the Russian-born in New York City,[82,83] upstate New York,[84] and the United States[85] noted that Jews comprise a high proportion of the Russian-born in the United States and confirmed an elevated risk of colon cancer in these populations. Socioeconomic status, urban residence, and country of origin may confound these observations; however, in the New York City study the excess of colon cancer among the Russian-born was seen in all socioeconomic strata with the highest relative risk among the higher classes. In the U.S. study the excess risk among the Russian-born was seen in both metropolitan and nonmetropolitan counties and in various regions of the country. Further studies of Jews would be useful to determine whether the elevated risk of colon cancer has persisted and to assess the role of diet and other factors.

Two small religious groups in the United States, the Seventh Day Adventists and members of the Church of Jesus Christ of the Latter-Day Saints (Mormons), have experienced a low risk of colorectal cancer. Adventists abstain from tobacco and alcohol and tend to avoid caffeine, sweets, and highly refined foods; approximately half are lacto-ovo-vegetarians. Compared to U.S. white males and females, Adventist males and females in California had SMRs of 0.58 and 0.52, respectively, during 1960–1976.[86,87] Among the cancers unrelated to smoking, colorectal cancer had the lowest ratios among Adventists of both sexes. The reduced risk among the California Adventists persisted when they were compared to non-Adventist Californians, of similar socioeconomic status, who chose to enroll in a study similar to the Adventist cohort study. On the other hand, Mormons avoid tobacco, alcohol, and caffeine; stress a balanced diet including grains, vegetables, and fruits; and eat meat in moderation. They do not, however, consume a diet especially low in total fat.[88,89] Yet compared to the data for U.S. whites in the cancer survey of 1969–1971, Mormon males and females in Utah had standardized incidence ratios of 0.62 and 0.62 for colon

cancer and 0.60 and 0.69, respectively, for rectal cancer during 1967–1975.[90] Mormon males and females in California had SMRs of 0.69 and 0.81 for colon cancer and 0.65 and 0.71 for rectal cancer during 1968–1975 compared to U.S. whites.[88]

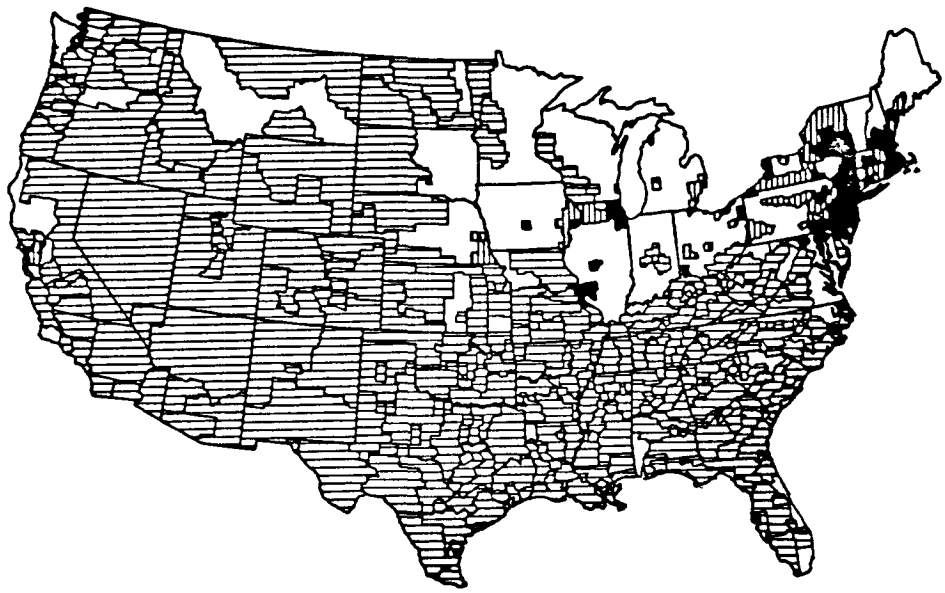
The reason for the reduced risk of colorectal cancer among Adventists and Mormons is not clear. In a cohort study of California Adventists, which included a limited dietary interview at entry into the study and 21 years of follow-up, no relationships of colorectal cancer mortality were seen with intake of meat, cheese, or milk, but some associations with egg consumption and body weight were noted.[91] Indices of fat and dietary fiber intake could not be formed. Among Mormons low fat intake cannot explain the low risk; further, per capita beef consumption in Utah, which is 72% Mormon, is higher than the U.S. level.[89] Recently, a population-based case–control study of colon cancer in the state of Utah, including both Mormons and non-Mormons, found a positive association with total caloric intake and a weak protective effect for fiber.[92] If these populations continue to maintain their 30% to 40% reduction in risk of colon cancer, more intensive research is justified to clarify the protective factors involved.

Regional Differences ■

The publication of cancer maps for the United States by the NCI revealed remarkable county-by-county variation in the age-adjusted (1960 U.S. standard) mortality rates for various forms of cancer.[93] Based on mortality data for white males and females during 1950–1969, the maps for both colon and rectal cancer showed relatively high rates in the Northeast (from Maine to Maryland) and in urban centers in the North Central states (from Ohio to Nebraska). Low rates were seen in the South (from Virginia to Florida and west to Texas), and intermediate rates in the West, with somewhat lower rates in the Southwest than in the Northwest. A similar pattern was seen in the corresponding maps among nonwhite men and women.[94]

Recently the cancer maps have been updated to include mortality by state economic area (SEA) for

FIG. 10–12 Age-adjusted (1960 U.S. standard) colorectal cancer mortality rates, 1970–1980 (excluding 1972), by state economic area for white males (U.S. rate = 23.7/100,000). Solid shading: in highest decile, significantly > U.S. rate; cross-hatching: in highest decile, not significantly > U.S. rate; vertical shading: not in highest decile, significantly > U.S. rate; horizontal shading: significantly < U.S. rate; blank: not significantly different from U.S. rate. State economic areas in the highest decile for men have colorectal cancer mortality rates $>28.3/10^5$. (See corrected map at end of article.)

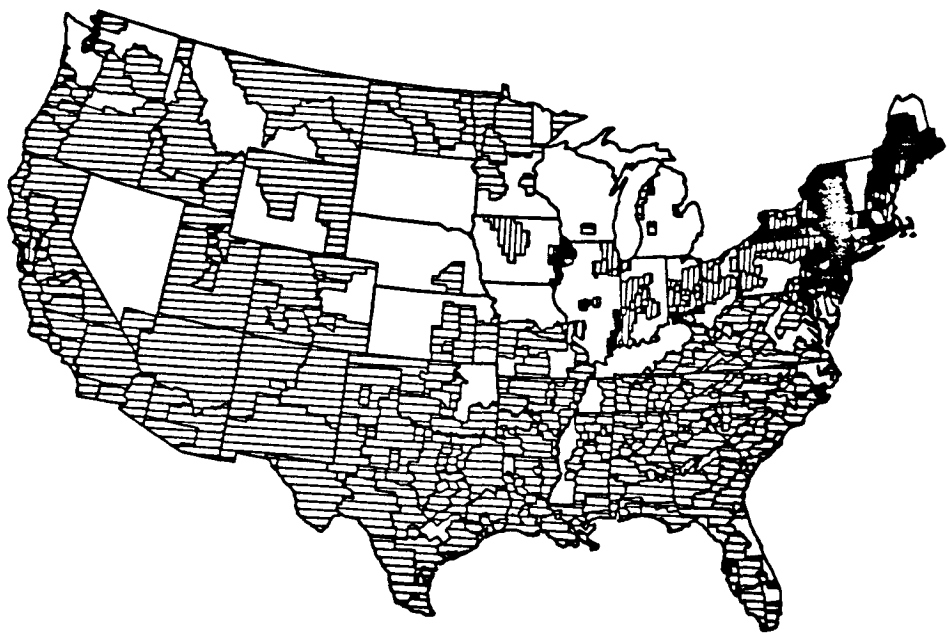


decades between 1950 and 1980.[95] The 506 SEAs in the United States are single counties or groups of counties that are relatively homogeneous with respect to demographic, economic, and climatic characteristics. Colon and rectal cancer are combined in this analysis because of the uncertainty involved in separating these sites on the basis of death certificate information and because of similar geographic patterns observed on the earlier maps.

The 1970–1980 maps for colorectal cancer in white males and females are shown in Figures 10–12 and 10–13. The regional patterns generally resemble those noted in the SEA maps prepared for 1950–1959 and 1960–1969 (not shown), but there are some changes. The high mortality rates in the Northeast persist, and an increased number of areas with elevated rates are seen in upstate New York, western Pennsylvania, Ohio, Indiana, and Illinois, especially for women. In the North Central region, which extends into Nebraska and Kansas, more areas have rates not significantly different from the U.S. average, compared to earlier decades when mortality was often significantly less than average in this region. In general, rates in the South remain significantly lower than U.S. rates, although a few more areas have rates not significantly different from the U.S. average, particularly in northern Virginia, eastern North Carolina, and Florida. Mortality in the West remains significantly lower than the U.S. average, and only the San Francisco Bay Area has rates similar to those of the Northeast and North Central states. It is noteworthy that an area of rural Nebraska that displayed elevated mortality rates in 1950–1969 appears unremarkable in the recent maps. A case–control study of colorectal cancer in this area revealed elevated risks among persons of Czech descent, who are concentrated there; it appears that the rates have declined with gradual acculturation of this migrant group.[96]

Despite the persistent geographic variation of colorectal cancer over time, the differentials are gradually fading. Among white males the generally high rates (age-adjusted using the 1960 U.S. standard) in the Northeast have declined, whereas the lower rates in the South have risen between 1950 and 1980; the

FIG. 10–13 Age-adjusted (1960 U.S. standard) colorectal cancer mortality rates, 1970–1980 (excluding 1972), by state economic area for white females (U.S. rate = 17.9/100,000). Solid shading: in highest decile, significantly > U.S. rate; cross-hatching: in highest decile, not significantly > U.S. rate; vertical shading: not in highest decile, significantly > U.S. rate; horizontal shading: significantly < U.S. rate; blank: not significantly different from U.S. rate. State economic areas in the highest decile for women have colorectal cancer mortality rates >21.4/10^5. (See corrected map at end of article.)



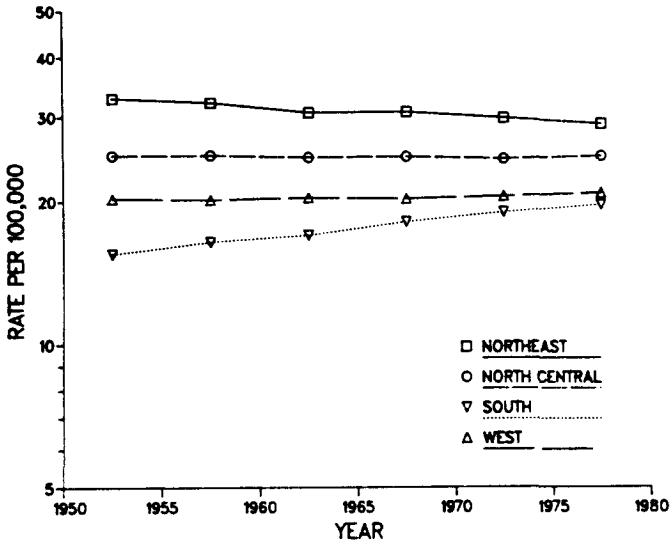


FIG. 10-14 Age-adjusted (1960 U.S. standard) regional trends in colorectal cancer mortality among white males in the United States, 1950–1979.

rates in the North Central and West regions have remained unchanged (Fig. 10-14). Among white females colorectal cancer mortality decreased in all four regions, with the sharpest decline in the Northeast and the weakest in the South (Fig. 10-15). Between 1950–1954 and 1976–1980 the ratio of colorectal cancer mortality in the Northeast relative to the South decreased from 2.1 to 1.5 among white males and from 1.7 to 1.4 among white females. For nonwhites also, regional differences have diminished, with the Northeast-South ratio declining from 2.1 to 1.4 among males and from 1.8 to 1.2 among females.

Geographic variation in colon and rectal cancer is also apparent in incidence data (Fig. 10-16). For 1978–1981, the highest rates for colon and rectal cancer in white males and females were in Connecticut, followed by other areas in the North (Detroit and Iowa) and San Francisco. In contrast, low risks were generally seen in Atlanta, New Mexico, and Utah.

The elevated risk of colorectal cancer in the Northeast and North Central states, relative to the South, may be influenced by the more extensive urbanization and higher socioeconomic status of these regions. Haenszel and Dawson[75] used 1949–1951 county mortality data for whites to demonstrate that in both metropolitan and nonmetropolitan counties colorectal cancer mortality rates were highest in the Northeast, followed successively by the North Central re-

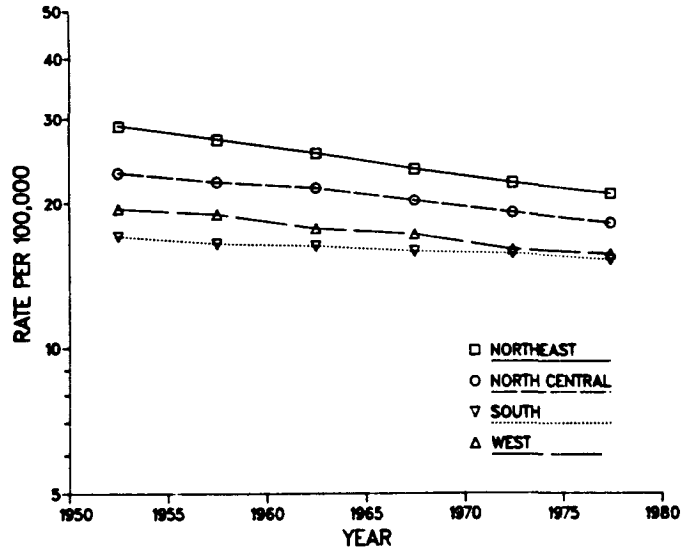


FIG. 10-15 Age-adjusted (1960 U.S. standard) regional trends in colorectal cancer mortality among white females in the United States, 1950–1979.

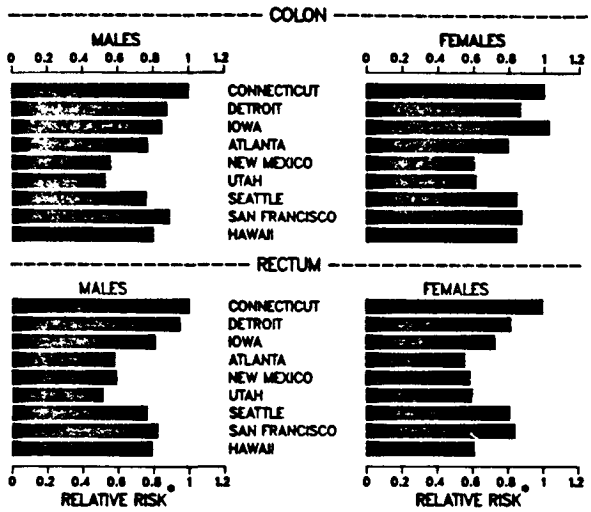


FIG. 10–16 Geographic variation in incidence of colon and rectum cancer among whites: SEER, 1978–1981. *All risks are expressed relative to the risks in Connecticut, based on age-adjusted (1970 U.S. standard) rates.[63]

gion, the Western states, and then the South. In a correlation study at the county level, Blot and colleagues[78] observed that population size, median income and education, and ethnicity were each independently related to risk of colorectal cancer, but they only partially explained the predominance of this cancer in the Northeast and North Central states, and its deficit in the South.

Regional differences in dietary patterns may be related to the North–South gradient in risk of colorectal cancer, but some investigators have recently suggested that natural sunlight may help explain the regional and urban–rural gradients. The proposed mechanism is that sunlight increases endogenous vitamin D production and thus enhances calcium absorption and biologic availability. Calcium ions in the large bowel may inhibit carcinogenic effects of ionized fatty acids and bile acids by forming insoluble calcium soaps.[24] Recent support for this hypothesis has come from a cohort study of Chicago factory workers, whose risk of colorectal cancer was found to be inversely related to the consumption of calcium and vitamin D.[97]

Florida Migrants ■

Once a North–South gradient in risk of colorectal cancer was identified in the United States, attention turned to the Southern retirement communities to see whether the migrants from the North acquired the reduced risk of the South. The U.S. cancer maps for 1950–1969 gave no indication that the mortality from colorectal cancer among whites in retirement areas of Florida, southern Arizona, or southern California was elevated above that of adjacent counties. To investigate this issue, 1970 census data were used to identify Florida counties with high rates of immigration from the Northeast and North Central states. The 11 counties were centered around Miami (southeast group), St. Petersburg (southwest group), and Orlando (northeast group). On the average, 44% of the U.S.-born white population of these counties were born in the Northeast or North Central states, and 16% of the total white population had resided in these two regions 5 years earlier.[98] To maintain comparability with the 11 Florida counties, Northern and Southern counties with populations >100,000 were used for comparison. Age-specific mortality curves for colorectal cancer in these three areas of Florida during 1950–1969 paralleled the mortality curves for other large Southern counties and did not rise toward Northern rates at any age, not even at the older retirement ages (Fig. 10–17). Similar results were seen for 1970–1975. Three explanations are possible for the low mortality rates reported in retirement areas. Most provocative is that a rapid reduction in risk occurs on migration to Florida, possibly owing to dietary changes, such as eating more vegetables and fruit. Second, a nonrepresentative subset of the Northern population chooses to migrate, and this group bears a low risk of colorectal cancer. Third, migrants are generally an unusually healthy group, since early symptoms of disease might discourage a change in residence. To explore these alternatives, age-specific mortality curves for several other cancers were prepared for the three Florida retirement areas and the Northern and Southern comparison counties. The curves for breast, pancreatic, and ovarian–uterine cancer resemble those for colorectal cancer. This suggests that part of the explanation for the apparent reduction in risk of colorectal cancer on migration to Florida is related to selection factors associated with migration.

A death certificate-based case–control study of colorectal cancer involving interviews of next-of-kin has recently been conducted in Florida retirement counties to assess directly whether there is a rapid reduction in risk on migration and to explore its characteristics.[99] Preliminary results indicate that increasing years of Florida residence for migrants from the Northeast and North Central states are not associated with decreasing risk of disease. Overall, if migration is from anywhere in the country, risk appears unrelated to age at migration; however, if migration is

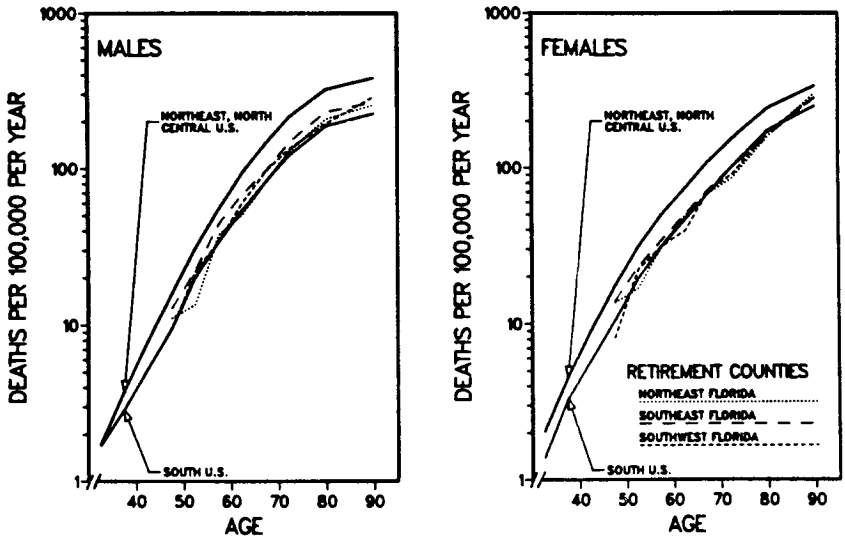


FIG. 10–17 Age-specific mortality from colorectal cancer in Florida retirement counties, northern U.S. counties, and southern U.S. counties among white males and females, 1950–1969.

from the North, the younger the age at migration to Florida, the lower is the risk of colorectal cancer. These results are shown in Table 10–5 for year-round Florida residents. The patterns are similar in men and women and also are seen among seasonal Florida residents. Adjusting for education, to ensure that the younger migrants were not at reduced risk because of lower socioeconomic status, did not change the results. Thus, our findings to date suggest that there is no rapid reduction in risk on moving to Florida among the older migrants but that those who migrated from the North at a young enough age appear to experience a decrease in risk. Migrating to Florida at age 35 years or younger confers more protection than migrating between 36 and 65 years, which in turn confers more protection than migrating at 66 years or older. Age at migration is crucial either because exposure to a new life-style has to be sustained for a long period or because the migrant has to be flexible enough to adopt a new life-style.

Implications of Recent Patterns ■

Many of the traditional demographic variables influencing the distribution of colorectal cancer in the United States, such as race and ethnicity, urbanization, region of the country, and perhaps socioeconomic status, appear to be decreasing in importance. During the 1970s colon and rectal cancer incidence rates among U.S. blacks, Japanese, and Chinese approached or slightly surpassed the rates prevailing among U.S. whites. The trends for Hispanic Americans, however, are mixed. The Hispanics in New Mexico, 94% of whom were U.S.-born in 1980,[100] seem to be retaining a substantially reduced risk of colon and rectal cancer (RR = 0.4–0.6), whereas the risks among Puerto Ricans living in New York City have moved closer in the migrating generation to the risk among U.S. whites. American Indians in New Mexico are also retaining a substantially lower risk of colon and rectal cancer relative to U.S. whites (RR

Table 10–5
Relative Risk* of Colorectal Cancer by Age at Migration to Florida

	Age at Migration				
Place of Origin	26–35	36–45	46–55	56–65	66–79
Northeast, North Central U.S.	1.0 (38, 39)†	1.3 (50, 39)	1.4 (96, 68)	1.3 (188, 152)	1.7 (104, 64)
All U.S.	1.0 (70, 52)	1.0 (93, 69)	0.9 (131, 103)	0.9 (230, 194)	1.1 (123, 82)

* All risks are relative to the 26–35 age group from the same place of origin.

† Numbers of cases and controls are in parentheses.

= 0.2–0.3). In addition, urban–rural gradients for colorectal cancer are decreasing over time, and socioeconomic status is not a consistent risk factor in the United States. For whites and blacks of both sexes the geographic gradient in risk of colorectal cancer has diminished, with the mortality ratios for the Northeast relative to the South dropping from 1.7–2.1 to 1.2–1.5 over the past 25 years. From the available data, it appears that Mormons and Seventh-Day Adventists maintain a reduced risk of colorectal cancer while Jews may still have an elevated risk, but further work is needed to assess trends in these groups.

In most segments of the U.S. population, however, the risks of colorectal cancer are tending to converge toward one another. Although the specific reasons remain uncertain, the trend is probably related to the increasing homogeneity of dietary patterns across the United States associated with the advent of refrigeration, national distribution of agricultural commodities, industrialization of food processing, food fortification programs, supermarkets, more meals eaten away from home, and fast-food restaurants. Because of the greater uniformity in cancer risks and dietary exposures, it will become more difficult to identify the responsible dietary and nutritional factors by studies of the U.S. general population; however, special opportunities for study are still afforded by populations with changing risks and exposures (*e.g.*, migrant groups) or with unusually high or low risks (*e.g.*, Mormons and Adventists).

The patterns of colorectal cancer in the United States are noteworthy in other ways. Over the past 30 years females have fared better than males. Incidence has remained steady among females and mortality has declined, whereas incidence has risen among males and mortality has leveled off. There is some evidence, however, that incidence rates for females have started in the past decade to rise in parallel with male rates. The reasons for the sex differences in risk deserve further study to clarify the role of diet, physical activity, and endogenous factors, which may affect bile composition, bowel transit time, and fecal weight and biochemistry.[101] The effects of parity and exogenous hormones also need further investigation. Population-based case–control studies in U.S. blacks,[71] U.S. whites,[102] and Australians[103] have shown a decreasing risk of colon cancer in women with increasing parity; in addition, a reduced risk in parous versus nulliparous women can be inferred from data in a Canadian study.[104] The Australian study, but not the study in U.S. whites, found a decreasing risk of colon cancer associated with earlier age at first birth and increasing use of oral contraceptives.[103] Cholecystectomy has been reported to increase the risk of right-sided colon cancer, particularly in females, but not all studies have confirmed this association.[105]

Another notable trend for colorectal cancer in the United States is the decreasing risk observed among men and women in the younger age groups, less than 45 years of age. At older ages the incidence has been declining less steeply and occasionally rising. Whether the pattern at younger ages reflects a cohort effect that will eventually influence all age groups is not known, but the trend should be carefully monitored and explored. A case–control study of younger as well as older adults with colorectal cancer may provide some explanation for this pattern. Case–control studies should also evaluate the risk factors according to segments of the large bowel, particularly in view of the recent increase of malignancies affecting the ascending and transverse colon. Although much research is currently focusing on dietary factors, genetic susceptibility should not be neglected, especially since the familial tendency to colorectal cancer is often manifested by right-sided and multicentric cancers, younger onset than usual, and accompanying polyps.[106,107]

Because of the limitations of dietary assessment in epidemiologic research, it is important, whenever possible, to link epidemiology with laboratory probes that will clarify the dietary components and mechanisms involved in the origins of colorectal cancer. It may be fruitful to focus also on adenomatous polyps, a precursor state that is less likely to alter the dietary and physiologic conditions leading to neoplasia. Whatever the study population, the prospects for gaining new etiologic insights will be greatly enhanced as observations move expeditiously from epidemiology to the laboratory, and *vice versa*, and as multidisciplinary groups collaborate to elucidate the causes of colorectal cancer and the means of prevention.

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Corrected figures 10-12 and 10-13

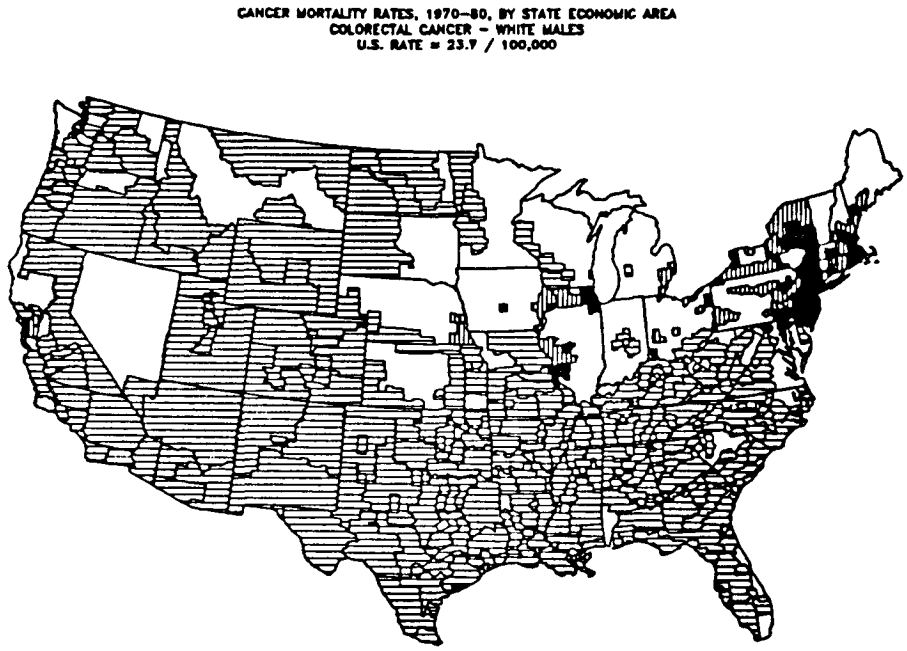

Figure 10-12

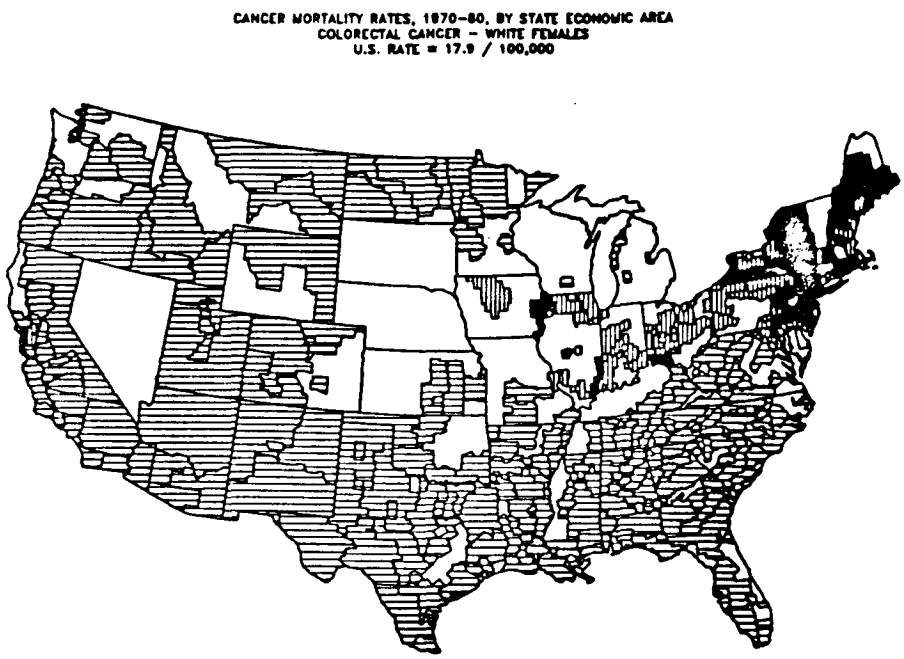

Figure 10-13